Sleep Medicine 15 (2014) 631–636

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Prognostic implication of obstructive sleep apnea diagnosed by post-discharge sleep study in patients presenting with acute coronary syndrome

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ARTICLE INFO

Article history:
Received 14 October 2013
Received in revised form 25 February 2014
Accepted 27 February 2014
Available online 13 April 2014

Keywords:
Sleep apnea
Acute coronary syndrome
Outcomes
Stents
Recovery period
Cardiovascular events

ABSTRACT

Objective: We aimed to determine the prognostic implications of obstructive sleep apnea (OSA) diagnosed during the recovery phase of acute coronary syndrome (ACS).
Methods: Patients presenting with ACS and treated with percutaneous coronary intervention were recruited prospectively for a home-based sleep study within 30 days of hospital discharge. Major adverse cardiac and cerebrovascular events (MACCEs) assessed included cardiac death, myocardial infarction, stroke, unplanned revascularization, and hospitalization for heart failure.
Results: Of the 85 patients recruited, 68 successfully completed the study. The median time from percutaneous coronary intervention to sleep study was 14 days (interquartile range: 7.5–27 days). OSA was diagnosed in 24 patients (35.3%) (apnea–hypopnea index $\geqslant$15). A drug-eluting stent was implanted into the target lesion in 45 patients (66.2%). None of the study patients had received treatment for OSA. At 24-month follow-up, the MACCE incidence was 34.9% in the OSA group and 5.1% in the non-OSA group ($P = 0.008$, log-rank test). After adjusting for the possible confounding effect of age, gender, coronary intervention indications, hypertension, smoking, and body mass index, OSA remained an independent predictor of MACCEs (adjusted hazard ratio, 6.95; 95% confidence interval, 1.17–41.4; $P = 0.033$).
Conclusion: OSA diagnosed in patients treated with percutaneous coronary intervention for ACS by post-discharge sleep studies conducted 2 weeks after percutaneous coronary intervention was independently associated with MACCEs at 24-month follow-up.

1. Introduction

In the past two decades, much research on obstructive sleep apnea (OSA) has focused on its association with cardiovascular disease, revealing and recognizing the vasculopathic effects of OSA [1–3]. Intermittent hypoxemia, intrathoracic pressure changes and arousal-induced reflex sympathetic activation have been implicated as the underlying pathophysiological mechanisms [3]. The enormous significance of these findings has completely changed sleep medicine. Several population surveys have shown that OSA is independently associated with an increased long-term risk of fatal and non-fatal cardiovascular events [4–6]. However, in patients presenting with acute coronary syndrome (ACS), the relationships between OSA and cardiovascular outcomes remain unclear, and the current data are limited and conflicting [7–9].

The reliability of diagnostic sleep studies performed during the acute phase of ischemic insults has been a major source of controversy surrounding the prognostic implications of OSA in ACS patients. Some data have described how sleep studies conducted at different times appear to affect OSA prevalence [10–12]. In a study of 18 patients admitted to coronary care units for a variety of cardiac conditions, OSA prevalence decreased from 56% during the acute phase to 18% at the six-week follow-up [10]. In 28 patients presenting with ACS and diagnosed with OSA during hospitalization, repeat sleep studies conducted at the six-month follow-up showed OSA resolution in 79% of patients [11]. A recent report showed that sleep studies performed during the acute phase of myocardial infarction functioned as independent predictors of

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http://dx.doi.org/10.1016/j.sleep.2014.02.009
1389-9457/

OSA [12]. These studies suggest that some of the OSA diagnosed during the acute phase of ACS may be transient, and that sleep studies should be performed during the recovery period to achieve better diagnostic accuracy.

Data on the relationships between OSA diagnosed during the ACS recovery period and subsequent cardiovascular outcomes have thus far been scarce. If a worse prognostic implication were demonstrated during recovery period diagnosis, it would further support the screening and treatment of OSA in patients presenting with ACS. Alternatively, OSA might merely be a marker of ACS. In this study, we sought to determine the prognostic implications of OSA diagnosed during the ACS recovery phase.

2. Methods

2.1. Study design and patient population

This was a single-center, prospective, observational study conducted at a tertiary institution in a multi-ethnic Asian country from February 2011 to December 2012. We recruited patients aged 21–80 years who were admitted to our institution for ACS and treated via percutaneous coronary intervention. We defined ACS as ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction or unstable angina according to the current standard clinical guidelines [13]. Patients with known OSA, who had received continuous positive airway pressure therapy or previous intervention treatment of the target vessel, who had experienced cardiogenic shock, chronic renal failure on dialysis or atrial fibrillation, or who were unable to provide informed consent were excluded. All of the recruited patients were scheduled to undergo a home-based overnight sleep study within 30 days of hospital discharge. The study was approved by the local institutional review board (National Healthcare Group Domain Specific Review Board; reference: C/2010/00341), and all of the subjects provided written informed consent.

2.2. Overnight sleep study

All of the sleep studies were performed using a portable level-3 diagnostic device (Embletta Gold, Natus Medical, Inc., Oakville, Ontario, Canada) that had been previously validated against full in-laboratory polysomnography [14]. The parameters measured included nasal airflow (nasal cannula), thoraco-abdominal movements (inductive respiratory bands), arterial oxygen saturation (pulse oximetry), snoring episodes derived from the integrated pressure transducer, limb movement, and body position (continuous actigraphy).

Outputs from the portable diagnostic device were analyzed by an investigator who was blinded to the patients' clinical characteristics. Apnea was defined as cessation of airflow for >10 s, and hypopnea was defined as 30–90% reduction in airflow from baseline lasting 10 s, in conjunction with desaturation of $\geqslant$4%. Apnea was classified as 'obstructive' if paradoxical thoraco-abdominal movement was detected, and 'central' if no thoraco-abdominal movement was present. Mean percutaneous blood oxygen saturation (SpO_2), lowest SpO_2 and total percentage of time $SpO_2 < 90\%$ were also recorded. As OSA was the sleep-disordered breathing of interest, patients with predominantly central sleep apnea were excluded from the analysis.

Each apnea–hypopnea index (AHI) was calculated as the total number of apneic and hypopneic episodes per hour of recording time in bed. The scoring was performed according to the American Academy of Sleep Medicine guidelines [15]. The recruited patients were classified into OSA (AHI $\geqslant$ 15) and non-OSA (AHI < 15) groups. OSA was defined as AHI $\geqslant$ 15 based on the latest clinical guidelines released by the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine [16].

2.3. Data collection and long-term follow-up

The following baseline demographic and clinical data were collected from the medical records of the recruited patients: gender, ethnicity, age, body mass index (BMI), cardiovascular risk factors (i.e. smoking, hypertension, hyperlipidemia, diabetes mellitus, family history of premature coronary artery disease), concomitant medical history (i.e. previous percutaneous coronary intervention, coronary artery bypass surgery, myocardial infarction, stroke, chronic renal failure), laboratory results, left ventricular ejection fraction, time from discharge to home sleep study, and discharge medications (i.e. aspirin, thienopyridine, beta blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, lipid-lowering therapy).

The follow-up period began from the time of percutaneous coronary intervention during the index hospital admission. The clinical outcomes of the patient cohort were conducted via clinical chart reviews and telephone calls by an investigator who was blinded to the patients' sleep results. All of the information was recorded prospectively. The outcomes were collected after 24-month follow-up. The MACCEs (cardiac death, myocardial infarction, unplanned revascularization, stroke, and hospital admission for congestive heart failure) comprised the primary endpoint of the study. All of the morbidities recorded were defined according to current standard guidelines.

2.4. Statistical analysis

The categorical variables were presented as numbers and percentages, and continuous variables were described as means with standard deviations or medians with ranges/interquartile ranges. Differences in the characteristics between the OSA and non-OSA groups were analyzed using the independent sample *t*-test for continuous data, or χ^2/Fisher's exact test for categorical data.

The MACCE cumulative incidence curves were constructed using the Kaplan–Meier method and compared using the log-rank test. A Cox proportional hazards multivariate analysis was performed to adjust for possible confounders such as age, gender, different ACS presentations (i.e. ST segment elevation myocardial infarction versus non-ST segment elevation myocardial infarction and unstable angina; the latter two categories were grouped together due to small number of unstable angina patients ($n = 3$)), hypertension, smoking and BMI. All of the statistical analyses were carried out using STATA v. 13 (StataCorp LP; College Station, TX, USA), assuming a two-sided test with a 5% level of significance.

3. Results

3.1. Baseline demographic and clinical characteristics

Eighty-five patients presenting with ACS were successfully recruited during their hospitalization periods and scheduled to undergo a home-based portable sleep study. Out of these 85 patients, 15 subsequently withdrew and defaulted the study. Among the 70 patients who underwent the study, 68 completed it successfully. Most of the study patients (86.8%) were male, and the average age was 54.2 ± 8.8 years.

Based on AHI $\geqslant$ 15, OSA was present in 24 patients (35.3%), whereas 44 patients (64.7%) were classified as non-OSA. None of the patients in the OSA group accepted continuous positive airway pressure therapy or any other treatments for OSA during the follow-up period. The baseline demographic and clinical characteristics of the patients are shown in Table 1. Patients in

the OSA group were less likely to be male, had a significantly higher BMI, showed a higher prevalence of hypertension but were less likely to be smokers. In terms of clinical presentations, there was a trend toward a lesser number of patients presenting with ST segment elevation myocardial infarction in the OSA group compared with the non-OSA group. The patients' baseline laboratory characteristics and left ventricular ejection fractions, assessed during the index hospitalization period, are presented in Table 2.

The procedural success of the percutaneous coronary interventions was achieved in all of the patients. None of the patients experienced any intervention-related complications. A drug-eluting stent was implanted into the target lesion in 66.2% of the patients, and the rates were similar between the OSA and non-OSA groups. Upon discharge from the index admission, all of the patients were prescribed medications in accordance with current international guidelines [17]. Aspirin was prescribed for 98.5% of the patients, thienopyridine for 100%, β-blockers for 88.2%, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers for 76.5%, and statins for 100% upon discharge. There were no significant differences in the medications prescribed between the OSA and non-OSA patients (data not shown).

3.2. Home-based overnight sleep study

The median time from percutaneous coronary intervention to home-based sleep study was 14 days (interquartile range, 7.5–27 days). The sleep study characteristics of our patients are reported in Table 3. The median AHI was 24.0 (range, 16.9–52.0) in the OSA patients and 4.9 (range, 0.3–14.9) in the non-OSA patients. The OSA patients scored significantly higher on the Epworth Sleepiness Scale (9.5 ± 3.3) compared with the non-OSA patients (7.1 ± 3.6).

3.3. Effect of OSA on long-term survival rate

Follow-up data were available for all 68 study patients. The median follow-up duration was 20 months (range, 4–30) and was similar in the OSA group (17.5; range, 4–30) and the non-OSA group (21; range, 7–30). During the study period, the OSA group incurred two myocardial infarctions, four unplanned revascularizations, two strokes, and one hospitalization for congestive heart failure in seven patients. The non-OSA group incurred one myocardial infarction and five unplanned revascularizations in three patients. No cardiac death was observed in the study population during the follow-up period. The median time to MACCE was 9 months (range, 4–23 months) and this was shorter in the OSA group (8 months, range: 4–19) compared to the non-OSA group (16 months; range, 7–23). The Kaplan–Meier cumulative incidence of MACCE curves for the OSA and non-OSA groups are presented in Fig. 1. The OSA group had a significantly higher MACCE rate than the non-OSA group after 24-month follow-up (34.9% versus 5.1%, respectively; $P = 0.008$; log-rank test). After adjusting for the possible confounding effect of age, gender, coronary intervention indications, hypertension, smoking, and BMI, OSA remained an independent predictor of MACCEs (adjusted hazard ratio: 6.95; 95% confidence interval: 1.17–41.4, $P = 0.033$); Table 4).

4. Discussion

We prospectively compared the MACCE rates between the OSA and non-OSA groups in a cohort of ACS patients treated with contemporary percutaneous coronary intervention. In contrast to earlier studies [8,9], OSA was diagnosed by a home-based sleep study conducted two weeks after percutaneous coronary intervention. The OSA prevalence was 35.3%. After 24-month follow-up, the patients in the OSA group showed a higher MACCE incidence than those in the non-OSA group. After adjusting for age, gender, clinical presentations, hypertension, smoking, and BMI, OSA remained independently associated with a higher MACCE rate.

The cardiovascular consequences of OSA have received increasing recognition in recent years. OSA is now considered a novel cardiovascular risk factor, as stated in the 2012 European guidelines on cardiovascular disease prevention in clinical practice [18]. Although multiple studies have shown a strong association

Table 1
Baseline demographic and clinical characteristics of study patients.

Characteristics	Overall ($n = 68$)	OSA (AHI ⩾ 15) ($n = 24$)	Non-OSA (AHI < 15) ($n = 44$)	P-value
Male sex, *n* (%)	59 (86.8)	18 (75.0)	41 (93.2)	0.034
Ethnicity, n (%)				0.395
Chinese	41 (60.3)	14 (58.3)	27 (61.4)	
Malay	13 (19.1)	7 (29.2)	6 (13.6)	
Indian	12 (17.6)	3 (12.5)	9 (20.5)	
Others	2 (2.9)	0	2 (4.5)	
Age (years), mean (SD)	54.2 (8.8)	56.7 (5.6)	52.8 (10.0)	0.083
BMI (kg/m^2), mean (SD)	25.5 (3.8)	27.5 (3.9)	24.4 (3.3)	<0.001
Cardiovascular risk factors, n (%)				
Smoking	32 (47.1)	4 (16.7)	28 (63.6)	<0.001
Hyperlipidemia	52 (76.5)	21(87.5)	31 (70.5)	0.113
Hypertension	33 (48.5)	16 (66.7)	17 (38.6)	0.027
Diabetes mellitus	17 (25.0)	9 (37.5)	8 (18.2)	0.079
Family history of premature CAD	24 (35.3)	7 (29.2)	17 (38.6)	0.435
Concomitant conditions, n (%)				
Previous myocardial infarction	8 (11.8)	5 (20.8)	3 (6.8)	0.120
Previous PCI	11 (16.2)	6 (25.0)	5 (11.4)	0.177
Previous CABG	0	0	0	–
Previous stroke/TIA	2 (2.9)	0	2 (4.5)	0.536
Chronic renal failure	1 (1.5)	1 (4.2)	0	0.353
Indication, n (%)				0.059
STEMI	38 (55.9)	9 (37.5)	29 (65.9)	
NSTEMI	27 (39.7)	13 (54.2)	14 (31.8)	
Unstable angina	3 (4.4)	2 (8.3)	1 (2.3)	

OSA, obstructive sleep apnea; AHI, apnea–hypopnea index; SD, standard deviation; BMI, body mass index; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; TIA, transient ischemic attack; STEMI, ST segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction.

Table 2
Baseline left ventricular ejection fraction and laboratory results.

Characteristics	Overall (n = 68)	OSA (AHI ⩾ 15) (n = 24)	Non-OSA (AHI < 15) (n = 44)	P-value
Left ventricular ejection fraction (%), mean (SD)	52 (12.2)	52 (13.9)	52 (11.4)	0.989
Cardiac markers[a]				
Peak creatine kinase (U/L), median (range)	2288 (73–10,788)	1743 (282–10,788)	2394 (73–7010)	0.744
Peak creatine kinase-MB (μg/L), median (range)	189.3 (3.0–300.0)	181.4 (11.2–300.0)	197.1 (3.0–300.0)	0.195
Peak troponin (μg/L), median (range)	77.4 (0.3–80.0)	54.1 (7.8–80.0)	80.0 (0.3–80.0)	0.345
Renal markers, mean (SD)				
Urea (mmol/L)	5.2 (1.5)	5.7 (1.6)	5.0 (1.5)	0.060
Creatinine (μmol/L)	80.0 (23.8)	86.0 (29.2)	76.7 (19.8)	0.124
Blood markers, mean (SD)				
White blood count ($\times 10^9$/L)	10.6 (3.4)	10.6 (0.8)	10.7 (0.5)	0.911
Hemoglobin (g/dL)	14.7 (1.4)	14.5 (1.6)	14.8 (1.2)	0.536
Platelet count ($\times 10^9$/L)	247.2 (55.5)	253.1 (60.2)	243.9 (53.1)	0.516
Lipid markers				
Total cholesterol (mmol/L), mean (SD)	5.0 (1.1)	4.9 (1.3)	5.0 (1.0)	0.619
Triglyceride (mmol/L), median (IQR)	1.5 (1.2–2.2)	1.46 (1.2–2.2)	1.53 (1.2–2.1)	0.888
Low density lipoprotein (mmol/L), mean (SD)	3.1 (1.0)	3.1 (1.1)	3.1 (0.9)	0.726
High density lipoprotein (mmol/L), mean (SD)	1.1 (0.3)	1.0 (0.2)	1.09 (0.3)	0.337
Glucose (mmol/L), mean (SD)	7.2 (4.6)	7.9 (5.1)	7.8 (4.3)	0.909

OSA, obstructive sleep apnea; AHI, apnea–hypopnea index; SD, standard deviation; IQR; interquartile range.
[a] Cardiac markers are presented for patients presenting with ST segment elevation myocardial infarction (n = 38) only.

Table 3
Sleep study characteristics.

Characteristics	Overall (n = 68)	OSA (AHI ⩾ 15) (n = 24)	Non-OSA (AHI < 15) (n = 44)	P-value
No. of days from PCI to sleep study, median (IQR)	14 (7.5–27)	10.5 (6–18)	18.5 (10–32)	0.059
AHI, median (range)	10.2 (0.3–52.0)	24.0 (16.9–52.0)	4.9 (0.3–14.9)	<0.001
Mean SpO_2, median (range)	95.5 (90.5–97.9)	94.3 (90.5–96.2)	95.8 (91.6–97.9)	<0.001
Lowest SpO_2, median (range)	87.0 (60.0–95.0)	82.5 (60.0–91.0)	89.0 (72.0–95.0)	<0.001
Total percentage of time SpO_2 < 90%, median (range)	0.2 (0–36.5)	2.1 (0–36.5)	0 (0–16.7)	<0.001
Epworth Sleepiness Scale, mean (SD)	7.9 (3.6)	9.5 (3.3)	7.1 (3.6)	0.008

OSA, obstructive sleep apnea; AHI, apnea–hypopnea index; PCI, percutaneous coronary intervention; IQR, interquartile range; SpO_2, percutaneous blood oxygen saturation; SD, standard deviation.

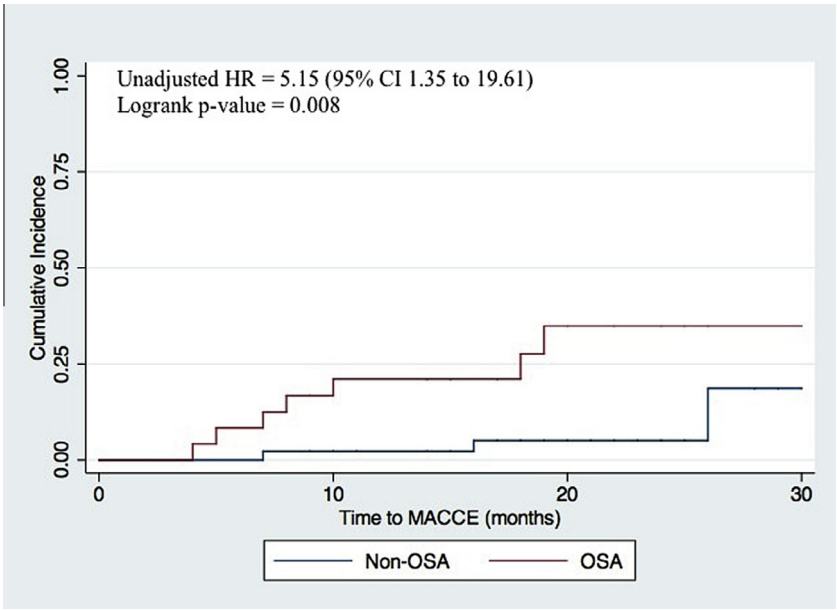

Fig. 1. Kaplan–Meier curve showing the cumulative major adverse cardiac and cerebrovascular event (MACCE) incidence in obstructive sleep apnea (OSA; red line) and non-OSA (blue line) patients. Unadjusted hazard ratio, 5.15 (95% confidence interval, 1.35–19.61); log-rank P = 0.008. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

between OSA and cardiovascular events in the general population [4–6], corresponding evidence in patients presenting with ACS have been limited and inconclusive. Two reported series found OSA to be an independent predictor of subsequent adverse cardiovascular events [7,8]. However, drug-eluting stents, the state-of-the-art treatment for ACS, were not used in these series.

Table 4
Multivariate Cox regression of MACCE-free survival.

Characteristics	Hazard ratio	95% CI	*P*-value
Presence of OSA	6.95	1.17–41.4	0.033
Age	1.04	0.93–1.16	0.529
STEMI indication	4.06	0.91–1.81	0.066
Male	0.31	0.06–1.73	0.183
Hypertension	3.00	0.54–16.86	0.211
Smoking	0.57	0.06–4.96	0.608
Body mass index	0.84	0.66–1.07	0.148

MACCE, major adverse cardiac and cerebrovascular event; CI, confidence interval; OSA, obstructive sleep apnea; STEMI, ST segment elevation myocardial infarction.

Moreover, the diagnostic sleep studies for OSA were performed during the acute phase in one study [8], but after hospital discharge in the other study [7]. In contrast, Mehra et al. reported a high prevalence of OSA in 104 ACS patients, but no association between OSA and any adverse outcomes was observed at the six-month follow-up [9]. There are several reasons for the discrepancy between the findings in Mehra's study and that in our study. Importantly, the study conducted by Mehra et al. utilized different endpoints of hospital readmission, emergency room visits, chest pain, dyspnea, paroxysmal nocturnal dyspnea, nocturnal angina, and palpitations in comparison to our study endpoints of cardiac death, myocardial infarction unplanned revascularization, stroke, and heart failure. The composite endpoints used in our study are standard clinical endpoints in cardiovascular research [19]. Although acute coronary syndrome is traditionally defined as 'acute myocardial infarction' or 'unstable angina', in the study by Mehra et al. 49% of all study patients presented with angina. As such, the study findings were not an accurate reflection of acute coronary syndrome patients. In addition, all recruited patients in Mehra's study underwent diagnostic sleep study within 72 h after hospital admission, which was during the acute phase of the cardiac event. This may have resulted in an overdiagnosis of OSA.

Recent evidence has suggested that the timing of sleep studies may influence OSA diagnosis in patients with ACS [12]. Although not immediately clear, this finding may be explained by the myocardial stunning and dysfunction experienced immediately following the acute ischemic event [20]. During the acute phase of ACS, a reduction in myocardial contractility may result in fluid retention. Consequently, patients may experience nocturnal rostral fluid shift, upper airway swelling and transient OSA [21]. Gradual recovery of myocardial contractility occurs after the acute phase, which usually takes seven days [22], accompanied by a resolution of the transient OSA experienced. Therefore, it has been proposed that some of the OSA diagnosed during the acute phase of ACS may be transient. Consistent with this notion, according to the post-discharge sleep study that we conducted 2 weeks after percutaneous coronary intervention, the prevalence of OSA was lower than that reported in two separate sleep studies conducted during the acute phase of ACS (35% versus 47.9% and 65.7%, respectively) [9,23].

One previous study reported the effects of OSA on outcomes by conducting sleep studies on patients at 7–14 days after percutaneous coronary intervention for ACS [7]. After a 7.5-month follow-up period, the target vessel revascularization rate of the OSA group was five times higher than that of the non-OSA group. However, there were a few caveats: only bare metal stents were used, and they were associated with a higher restenosis rate compared with drug-eluting stents. The widespread adoption of drug-eluting stents in recent years might have made the prognostic implications of OSA more difficult to demonstrate [24]. The results of our study were based on the use of contemporary percutaneous coronary intervention devices. Together with the longer follow-up duration in our study (24 versus 7.5 months), our findings provide an up-to-date paradigm on the prognostic implication of OSA.

Smoking status and male gender were adjusted for as possible confounders of MACCE. Although both factors were not significant predictors of MACCE in the multivariate analysis, smoking and male gender were both associated with a reduced adjusted hazard ratio. This is contrary to current theories implicating a worse prognosis with smoking. The result may be attributed to the significantly lower percentage of current smokers in the OSA group rather than to an independent protective effect of smoking on MACCE. Although male gender is an established risk factor for OSA, whether gender exerts an effect as a predictor of MACCE in OSA patients remains uncertain. An establishment of the relationship of gender on cardiovascular outcomes in OSA patients is precluded by a paucity of studies specific to the evaluation of gender differences [4–6,25]. Future studies specific to the investigation of smoking and gender effects on cardiovascular outcomes in OSA patients are warranted. Nevertheless, we have adjusted for them as possible confounders in our study, and the presence of OSA remained an independent predictor of MACCE.

To our knowledge, this is the first study to report on the relationship between OSA diagnosed during the ACS recovery period and cardiovascular outcomes in patients treated with contemporary percutaneous coronary intervention. In our cohort of ACS patients, we found the MACCE rate in the OSA group to be almost seven times higher than that in the non-OSA group. Several non-randomized studies among community individuals with OSA have reported decreased adverse event rates with OSA treatment via continuous positive airway pressure [4,26,27]. Further, a retrospective study reported that, in cardiac patients undergoing percutaneous coronary intervention, those treated for OSA had a significantly decreased number of cardiac deaths at the five-year follow-up compared with untreated OSA patients (3% versus 10%; $P = 0.027$) [28]. Taken as a whole, it seems reasonable to suggest that patients with ACS should be screened for OSA, and that continuous positive airway pressure should be offered to OSA patients.

4.1. Limitations

Our findings must be interpreted in the light of this study's limitations. The small sample size precluded a conclusive statement of our results, accounting for the wide confidence intervals observed in the multivariate results for the prevalence of OSA. For the same reason, it was not appropriate to conduct a subgroup analysis based on the patients' different clinical presentations. We excluded the recruitment of severely ill ACS patients and those with an inability to give consent. It is possible that OSA may exert a more pronounced effect in such patients. After providing informed consent in the hospital, 15 of the 85 recruited patients (18%) failed to carry out the sleep study. Most of the patients who withdrew expressed hesitancy and a reluctance to allow a sleep technician to enter their homes to set up the portable sleep device. Whereas there were no differences between the OSA and non-OSA groups in terms of their medications upon discharge, we did not capture data on compliance and subsequent prescriptions during the follow-up period. All patients diagnosed with OSA were given the option to visit the sleep clinic. However, none of the patients took up this option. As systemic referral for continuous positive airway pressure therapy is not included as a standard practice in the treatment of acute coronary syndrome, we did not actively refer patients diagnosed with OSA to the sleep clinic. Unfortunately, the exact reasons for refusal were not captured in the present study. The follow-up period of 24 months may not have been long enough to document the effects of OSA on cardiac mortality.

5. Conclusion

In a cohort of patients treated with percutaneous coronary intervention for ACS using mainly drug-eluting stents, OSA diagnosed by a home-based sleep study conducted two weeks after index percutaneous coronary intervention was found to be independently associated with subsequent MACCEs. The lower prevalence of OSA in this study compared with previous reports suggests the presence of transient OSA during the acute phase of ACS. These findings should influence future research efforts. Randomized controlled studies that evaluate the effect of OSA treatment on MACCEs are warranted.

Funding source

This study was funded by the Academic Research Fund (Grant No. R172-000-239-112) of the Ministry of Education, Singapore.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.02.009.

Acknowledgements

The authors gratefully acknowledge Miss Agnes Chow, Director of Avatton Medical, for her assistance with the home-based sleep study; Miss Pei-Ee Lee and Miss Venesa Loh for their help with patient recruitment; and the Sleep Laboratory at the National University Hospital in Singapore for their analysis of the sleep tracings.

References

[1] Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet 2009;373:82–93.
[2] Jaffe LM, Kjekshus J, Gottlieb SS. Importance and management of chronic sleep apnoea in cardiology. Eur Heart 2013;34:809–15.
[3] Kohler M, Stradling JR. Mechanisms of vascular damage in obstructive sleep apnea. Nat Rev Cardiol 2010;7:677–85.
[4] Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnea–hypopnea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365:1046–53.
[5] Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep 2008;31:1071–8.
[6] Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009;6:e1000132.
[7] Yumino D, Tsurumi Y, Takagi A, Suzuki K, Kasanuki H. Impact of obstructive sleep apnea on clinical and angiographic outcomes following percutaneous coronary intervention in patients with acute coronary syndrome. Am J Cardiol 2007;99:26–30.
[8] Lee CH, Khoo SM, Chan MY, Wong HB, Low AF, Phua QH, et al. Severe obstructive sleep apnea and outcomes following myocardial infarction. J Clin Sleep Med 2011;7:616–21.
[9] Mehra R, Principe-Rodriguez K, Kirchner HL, Strohl KP. Sleep apnea in acute coronary syndrome: high prevalence but low impact on 6-month outcome. Sleep Med 2006;7:521–8.
[10] Skinner MA, Choudhury MS, Homan SD, Cowan JO, Wilkins GT, Taylor DR. Accuracy of monitoring for sleep-related breathing disorders in the coronary care unit. Chest 2005;127:66–71.
[11] Schiza SE, Simantirakis E, Bouloukaki I, Mermigkis C, Kallergis EM, Chrysostomakis S, et al. Sleep disordered breathing in patients with acute coronary syndromes. J Clin Sleep Med 2012;8:21–6.
[12] Low TT, Hong WZ, Tai BC, Hein T, Khoo SM, Tan AY, et al. The influence of timing of polysomnography on diagnosis of obstructive sleep apnea in patients presenting with acute myocardial infarction and stable coronary artery disease. Sleep Med 2013;14:985–90.
[13] Simoons ML, Boersma E, van der Zwaan C, Deckers JW. The challenge of acute coronary syndromes. Lancet 1999; 353(Suppl. 2):SII1–4.
[14] Dingli K, Coleman EL, Vennelle M, Finch SP, Wraith PK, Mackay TW, et al. Evaluation of a portable device for diagnosing the sleep apnoea/hypopnoea syndrome. Eur Respir J 2003;21:253–9.
[15] Iber C, Ancoli-Israel S, Chesson AL, Quan SF. AASM manual for the scoring of sleep and associated events: rules, terminology and technical specification. Westchester, IL: American Academy of Sleep Medicine; 2007.
[16] Epstein LJ, Kristo D, Strollo Jr PJ, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5:263–76.
[17] Krumholz HM, Anderson JL, Bachelder BL, Fesmire FM, Fihn SD, Foody JM, et al. ACC/AHA 2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to develop performance measures for ST-elevation and non-ST-elevation myocardial infarction): developed in collaboration with the American Academy of Family Physicians and the American College of Emergency Physicians: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, Society for Cardiovascular Angiography and Interventions, and Society of Hospital Medicine. Circulation 2008;118:2596–648.
[18] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European guidelines on cardiovascular disease prevention in clinical practice (version 2012): the Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention and Rehabilitation (EACPR). Eur Heart J 2012;33:1635–701.
[19] Hicks KA, James Hung HM, Mahaffey KW, et al. on behalf of the Standardized Data Collection for Cardiovascular Trials Initiative. Standardized definitions for end point events in cardiovascular trials. Published October 20; 2010. Available at: http://www.cdisc.org/stuff/contentmgr/files/0/2356ae38ac190ab8ca4ae0b222392b37/misc/cdisc_november_16__2010.pdf [accessed December 2013].
[20] Camici PG, Prasad SK, Rimoldi OE. Stunning, hibernation, and assessment of myocardial viability. Circulation 2008;117:103–14.
[21] Yumino D, Redolfi S, Ruttanaumpawan P, Su MC, Smith S, Newton GE, et al. Nocturnal rostral fluid shift: a unifying concept for the pathogenesis of obstructive and central sleep apnea in men with heart failure. Circulation 2010;121:1598–605.
[22] Thygesen K, Alpert JS, White HD. Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. Universal definition of myocardial infarction. Eur Heart J 2007;28:2525–38.
[23] Lee CH, Khoo SM, Tai BC, Chong E, Lau C, Than Y, et al. Obstructive sleep apnea in patients admitted for acute myocardial infarction. Prevalence, predictors, and effect on microvascular perfusion. Chest 2009;135:1488–95.
[24] Topol EJ, Nissen SE. Our preoccupation with coronary luminology: the dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995;92:2333–42.
[25] Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I, Almeida-Gonzalez C, Catalan-Serra P, Montserrat JM. Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med 2012;156:115–22.
[26] Doherty LS, Kiely JL, Swan V, McNicholas WT. Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest 2005;127:2076–84.
[27] Milleron O, Pilliere R, Foucher A, de Roquefeuil F, Aegerter P, Jondeau G, et al. Benefits of obstructive sleep apnoea treatment in coronary artery disease: a long-term follow-up study. Eur Heart J 2004;25:728–34.
[28] Cassar A, Morgenthaler TI, Lennon RJ, Rihal CS, Lerman A. Treatment of obstructive sleep apnea is associated with decreased cardiac death after percutaneous coronary intervention. J Am Coll Cardiol 2007;50:1310–4.